

IN THE CLAIMS

1. (Currently amended) A method for an agent that modulates bone mineralization, said method comprising:

contacting an osteogenic cell expressing a NELL-1 gene with a test agent; and detecting an expression level of said NELL-1 gene in the contacted cell, where a difference in the expression level of NELL-1 in ~~a~~ an osteogenic cell that is not contacted indicates that said test agent is an agent that modulates bone mineralization,

wherein the osteogenic cell is selected from the group consisting of an osteoblast, a mesenchymal cell, a fibroblast cell, a dura cell, a chondrocyte, a MC3T3 cell and a chondroblast.

2. (Previously amended) The method of claim 1, further comprising recording test agents that modulate expressions of the NELL-1 nucleic acid or NELL-1 protein in a database of test agents modulating NELL-1 activity or in a database of test agents modulating bone mineralization.

3. (Withdrawn) The method of claim 1, wherein the expression level of is detected by measuring the level of *NELL-1* mRNA in said cell.

4. (Withdrawn) The method of claim 3, wherein said level of *NELL-1* mRNA is measured by hybridizing said mRNA to a probe that specifically hybridizes to a *NELL-1* nucleic acid.

5. (Withdrawn) The method of claim 4, wherein said hybridizing is according to a method selected from the group consisting of a Northern blot, a Southern blot using DNA derived from the Nell-1 RNA, an array hybridization, an affinity chromatography, and an *in situ* hybridization.

6. (Withdrawn) The method of claim 5, wherein said probe is a member of a plurality of probes that forms an array of probes.

7. (Withdrawn) The method of claim 3, wherein said wherein said level of *NELL-1* mRNA is measured using a nucleic acid amplification reaction.

8. (Original) The method of claim 1, wherein said level of *NELL-1* is detected by determining the expression level of a *NELL-1* protein in said biological sample.

9. (Original) The method of claim 8, wherein said detecting is via a method selected from the group consisting of capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, and immunohistochemistry.

10. (Original) The method of claim 1, wherein said cell is cultured *ex vivo*.

11. (Original) The method of claim 1, wherein said test agent is not an antibody.

12. (Original) The method of claim 1, wherein said test agent is not a protein.

13. (Withdrawn) A method of prescreening for modulator of a *NELL-1*, said method comprising:

(a) contacting a *NELL-1* nucleic acid or a *NELL-1* protein with a test agent; and
(b) detecting specific binding of said test agent to said *NELL-1* protein or nucleic acid.

14. (Withdrawn) The method of claim 13, further comprising recording test agents that specifically bind to said *NELL-1* nucleic acid or to said *NELL-1* protein in a database of candidate modulators of *NELL-1* activity or in a database of candidate modulators of bone mineralization.

15. (Withdrawn) The method of claim 13, wherein said test agent is not an antibody.

16. (Withdrawn) The method of claim 13, wherein said test agent is not a protein.

17. (Withdrawn) The method of claim 13, wherein said detecting comprises detecting specific binding of said test agent to said *NELL-1* nucleic acid.

18. (Withdrawn) The method of claim 17, wherein said binding is detected using a method selected from the group consisting of a Northern blot, a Southern blot using DNA derived from the *Nell-1* RNA, an array hybridization, an affinity chromatography, and an *in situ* hybridization.

19. (Withdrawn) The method of claim 13, wherein said detecting comprises detecting specific binding of said test agent to said *NELL-1* protein.

20. (Withdrawn) The method of claim 19, wherein said detecting is via a method selected from the group consisting of capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, and immunohistochemistry.

21. (Withdrawn) The method of claim 13, wherein said test agent is contacted directly to the *NELL-1* nucleic acid or to the *NELL-1* protein.

22. (Withdrawn) The method of claim 13, wherein said test agent is contacted to a cell containing the *NELL-1* nucleic acid or the *NELL-1* protein.

23. (Withdrawn) The method of claim 22, wherein said cell is cultured *ex vivo*.

24. (Withdrawn) The method of claim 13, wherein said test agent is contacted to an animal comprising a cell containing the *NELL-1* nucleic acid or the *NELL-1* protein.

25. (Withdrawn) A method of increasing bone mineralization, said method comprising increasing the concentration of a *NELL-1* gene product in an osteogenic cell.

26. (Withdrawn) The method of claim 25, wherein said increasing the concentration of *NELL-1* gene product comprises upregulating expression of a *NELL-1* gene.

27. (Withdrawn) The method of claim 26, wherein said upregulating comprises upregulating expression of an endogenous *NELL-1* gene.
28. (Withdrawn) The method of claim 26, wherein said upregulating comprises transfecting said cell with a vector that expresses a *NELL-1* protein.
29. (Withdrawn) The method of claim 28, wherein said vector constitutively expresses a *NELL-1* protein.
30. (Withdrawn) The method of claim 28, wherein expression of a *NELL-1* protein by said vector is inducible.
31. (Withdrawn) The method of claim 25, wherein said increasing the concentration of *NELL-1* gene product comprises contacting the bone with a *NELL-1* polypeptide.
32. (Withdrawn) The method of claim 28, wherein said osteogenic cell is selected from the group consisting of a mature osteoblast, osteoblast, a mesenchymal cell, a fibroblast cell, a fetal embryonic cell, a stem cell, a bone marrow cell, a dura cell, a chondrocyte, and a chondroblast.
33. (Withdrawn) A method of facilitating the repair of bone fractures, said method comprising increasing concentration of a *NELL-1* gene product at or near the fracture site.
34. (Withdrawn) The method of claim 33, wherein the gene product is increased in an osteogenic or bone precursor cell present at or near the fracture site.
35. (Withdrawn) The method of claim 33, comprising introducing an osteogenic cell or bone precursor cell that overexpresses *NELL-1* into said fracture site.
36. (Withdrawn) The method of claim 34, comprising increasing the concentration of a *NELL-1* gene product in said osteogenic cell or said bone precursor cell *in situ*.

37. (Withdrawn) The method of claim 34, wherein said increasing the concentration of *NELL-1* gene product comprises upregulating expression of a *NELL-1* gene in said osteogenic cell.

38. (Withdrawn) The method of claim 34, wherein said upregulating comprises upregulating expression of an endogenous *NELL-1* gene in said osteogenic cell.

39. (Withdrawn) The method of claim 37, wherein said upregulating comprises transfecting said cell with a vector that expresses a *NELL-1* protein.

40. (Withdrawn) The method of claim 39, wherein said vector constitutively expresses a *NELL-1* protein.

41. (Withdrawn) The method of claim 39, wherein expression of a *NELL-1* protein by said vector is inducible.

42. (Withdrawn) The method of claim 33, wherein said increasing the concentration of *NELL-1* gene product comprises contacting the cell with a *NELL-1* polypeptide.

43. (Withdrawn) The method of claim 34, wherein said osteogenic cell is selected from the group consisting of a mature osteoblast, osteoblast, a mesenchymal cell, a fibroblast cell, a fetal embryonic cell, a stem cell, a bone marrow cell, a dura cell, a chondrocyte, and a chondroblast.

44. (Withdrawn) A method of facilitating the repair of a bone fracture, said method comprising contacting the bone fracture site with a *NELL-1* protein.

45. (Withdrawn) The method of claim 44, wherein said *NELL-1* protein is combined with a collagen.

46. (Withdrawn) A bone graft material capable of enhancing the formation of osseous tissue in the animal in which it is implanted, said bone graft material consisting essentially of a biocompatible matrix and a NELL-1 protein.

47. (Withdrawn) The graft material of 46, wherein said graft material is resorbable.

48. (Withdrawn) The graft material of 46 wherein said NELL-1 is produced by a cell within said matrix expressing exogenous NELL-1 protein.

49. (Withdrawn) A bone graft material capable of inducing the formation of osseous tissue in the animal in which it is implanted, said bone graft material consisting essentially of a collagen conjugate containing:

from about 65 to about 95 weight percent reconstituted collagen; and

from about 35 to about 5 weight percent of NELL-1 protein.

50. (Withdrawn) The method of claim 1, wherein the osteogenic cell is selected from the group comprising an osteoblast, a mesenchymal cell, a fibroblast cell, a fetal embryonic cell, a stem cell, a bone marrow cell, a dura cell, a chondrocyte, a chondroblast, fetal calvarial osteoblastic cell, or a MC3T3 cell.

51. (Currently amended) The method of claim 1, wherein the osteogenic cell is ~~selected~~ from a cell endogenous to a fetal calvarial cell culture.

52. (Currently amended) A method for an agent that modulates bone mineralization, said method comprising:

contacting an osteogenic cell endogenous to a fetal calvarial cell culture expressing a NELL-1 gene with a test agent; and detecting an expression level of said NELL-1 gene in the contacted cell, where a difference in the expression level of NELL-1 in an osteogenic cell that is not contacted indicates that said test agent is an agent that modulates bone mineralization,

~~The method of claim 51, wherein the osteogenic cell is selected from the group comprising an osteoblast, a mesenchymal cell, a fibroblast cell, a stem cell, or a bone marrow cell, a dura cell, a chondrocyte, and a chondroblast.~~

53. Canceled.

54. (New) A method for an agent that modulates bone mineralization, said method comprising:

contacting an osteogenic cell expressing a NELL-1 gene with a test agent; and detecting an expression level of said NELL-1 gene in the contacted cell, where a difference in the expression level of NELL-1 in an osteogenic cell that is not contacted indicates that said test agent is an agent that modulates bone mineralization.